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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,320	11/03/2005	Yoshiko Takayama	2005_1592A	1755

513 7590 02/03/2011

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EXAMINER	
HUANG, GIGI GEORGIANA	

ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
02/03/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/553,320	TAKAYAMA ET AL.	
	Examiner	Art Unit	
	GIGI HUANG	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-16 and 18-20* is/are pending in the application.

4a) Of the above claim(s) *14-16 and 18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The response filed November 19, 2010 has been received, entered and carefully considered. The response affects the instant application accordingly:

a. Claim 13 has been amended.

2. Claims 13-16, 18-20 are pending in the case.

3. Claim 13 is present for examination.

4. New grounds of rejection are set forth in the current office action as a result of amendment.

New Grounds of Rejection

Due to the amendment of the claims the new grounds of rejection are applied:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claim 13 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Hellberg et al. (WO 03/020281) in view of McKerracher et al. (WO 99/23113) and Hara et al. (Protein kinase inhibition by fasudil hydrochloride promotes neurological recovery after spinal cord injury in rats).

Hellberg et al. teaches the use of compounds that promote neuron regeneration or neurite outgrowth for the treatment of conditions from injury (damage) to the corneal

nerve such as after surgeries or trauma, including dry eye and other conditions related to corneal nerve damage (e.g. corneal sensitivity after LASIK) encompassing the conditions of claim 13 (Abstract, Page 4 line 19-22, Page 5 line 8-25, Page 6 line 18-23). The compounds are used promote neurite outgrowth or regenerate severed neurons, examples include bFGF(basic fibroblast growth factor), NGF (Nerve growth factor), neotrofin, idebenone, and clenbuternol (see full document, specifically Abstract, Page 4 line 16-Page 5 line 25, Page 6 line 12-23, Claim 1-4, 7-10, 13-16).

Hellberg et al. do not expressly teach the use of Rho kinase inhibitors such as fasudil hydrochloride, but does teach the utility of compounds that promote neuron regeneration or neurite outgrowth (neuritogenesis) for addressing corneal nerve damage from conditions such as corneal surgery.

McKerracher et al. teaches that Rho antagonists (Rho kinase inhibitors- e.g. C3) are effective agents for blocking myelin inhibition and stimulate axon growth and neurite outgrowth (neuritogenesis)(Abstract, Page line 10-20, Page 7 line 4-12). McKerracher also teaches that these Rho inhibitors are useful for treating conditions and ailments of the peripheral nervous system (PNS) and central nervous system (CNS) by increasing neurite extension, growth, or regeneration (Page15 line 6-15) . This includes spinal cord injuries and ophthalmic neurons as demonstrated by its application to retinal neurons and crushed optic nerves (Page 8 line 25-Page 9 line 2, Figure 5 and 7, Page 9 line 13-Page 10 line 18, Page 12 line 11-24, Page 29-34, Claim 22).

Hara et al. teaches that fasudil hydrochloride (HA1077, Rho kinase inhibitor) can promote neurological recovery after traumatic spinal cord injuries (SCI) as are other

agents such as neurotrophic factors known in the art that improve neurological recovery in SCI (Introduction-Page 94, e.g. basic fibroblast growth factor-citation 5, Nerve growth factor-citation 16, 31, 44,) .

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to utilize fasudil hydrochloride to promote neuron regeneration/neurite outgrowth for corneal injury from condition such as corneal surgery, as suggested by McKerracher and Hara, and produce the instant invention as it is *prima facie* obvious for one of ordinary skill in the art to use another neurite promoter such as fasudil for corneal injury as Hellberg et al. teaches the use of compounds that promote neuron regeneration or neurite outgrowth for corneal disorders including corneal nerve damage from surgery, and Hara et al. teaches that fasudil (a known Rho kinase inhibitor) was an effective neuropromoter that recovered injured spinal neurons (spinal cord injury) and McKerracher teaches that the Rho inhibitors are neuron regenerators/promoters useful for PNS and CNS conditions like spinal cord injuries and retinal/optic neurons. Hara also addresses that neuropromotion was with fasudil and other neurotrophic factors which are the same ones in Hellberg, wherein they are functionally useful (equivalent). Wherein not only is it obvious to incorporate and utilize a known neurite/neuron promoter (fasudil) for the same purpose as similar neurite/neuron promoters (neurotrophic factors) for a specific treatment (corneal nerve damage) when they have both been effective for a similar conditions and/or therapeutic result (neurological recovery of spinal cord injuries) with a reasonable expectation of success; it is also obvious to use a Rho inhibitor such as fasudil which is an effective

and useful neuropromoter/regeneration (Hara), for a condition such as corneal injury where the treatment utilized compounds that can promote neuron regeneration or neurite outgrowth which encompasses Rho inhibitors like fasudil (Hellberg) and are taught to be useful for PNS and CNS conditions (McKerracher).

One of ordinary skill in the art would have been motivated to do this because it is desirable to use a known compound such as fasudil hydrochloride with known properties for promoting axon extension and regeneration, to treat the same conditions as another neurite/neuron promoters such as neurotrophic factors (e.g. bFGF, NGF) when it is they are both effective to treat neurological damage. It is desirable to have additional compounds that are effective neuropromoters for a treatment of corneal injury that utilizes neuropromoters as it is desirable for manufacturers to have different compounds useful for the same purpose and to have new methods of treatment for a known compound which allows for new sales.

Response to Arguments

Applicant's arguments filed 11/19/2010 have been fully considered but they are not persuasive. Applicant's arguments are centered on the assertions against the references individually, where one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. Additionally, the assertion that one of ordinary skill in the are would not have been motivated to substitute a neurotrophic factor with a Rho kinase inhibitor with a reasonable expectation of success even if the neurotrophic factor was effective is fully considered but not persuasive as the rejection is directed to the inclusion of the Rho

inhibitor rather than its substitution for the neurotrophic factors, and Hellberg is clear on the utilization of compounds that can promote neuron regeneration/neurite outgrowth for addressing corneal nerve damage from various conditions including corneal surgery.

These include neurotrophic factors (e.g. bFGF, NGF) and McKerracher teaches that the Rho inhibitors are neuron regenerators/promoters useful for PNS and CNS conditions like spinal cord injuries and retinal/optic neurons where it is obvious to one of skill in the art incorporate Rho inhibitors as they shown to be capable of performing the same neuronal outgrowth/regeneration addressed by Hellberg and Hara also addresses that neuropromotion was with fasudil (a Rho kinase inhibitor) and other neurotrophic factors which are the same ones in Hellberg, were are functionally useful (equivalent) such that not only is it obvious to incorporate and utilize a known neurite/neuron promoter (Rho kinase inhibitors) for the same purpose as similar neurite/neuron promoters (neurotrophic factors) for a specific treatment (corneal nerve damage) when they have both been effective for a similar conditions and/or therapeutic result (neurological recovery of spinal cord injuries) with a reasonable expectation of success; but it is also obvious to use a Rho inhibitor such as fasudil which is an effective and useful neuropromoter/regeneration and functionally equivalent to those already addressed by Hellberg (Hara) as there is a reasonable expectation of success as the Rho inhibitors are addressed to have the ability to produce neuritogenesis for the eye (McKerracher).

Accordingly, the rejection stands.

Conclusion

6. Claim 13 is rejected.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GIGI HUANG whose telephone number is (571)272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, FEREYDOUN SAJJADI can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GiGi Huang/
Examiner, Art Unit 1617
/Zohreh A Fay/
Primary Examiner, Art Unit 1627